Remarks

The claims are 18, 19, 22, 23, and 33. The Examiner included claim 28 as pending in the last Office Action (Paper No. 37) but the claim was cancelled in Applicants' response filed on July 16, 2001 (Paper No. 20). New claim 33 finds support in currently amended claim 18. Claims 20 and 29 have been cancelled. Applicants reserve the right to prosecute these claims in a continuing application.

Double Patenting
Applicants request that the rejection of claims 18-20, 22, 23, and 29 with regard to double patenting be withdrawn as the parent application (USSN 08/848,439) is now abandoned.

Claim Rejections – 35 U.S.C. §101
Claims 18-20, 22, 23, and 29 have been rejected under 35 U.S.C. §101. The Examiner cites Shirozu et al. (Genomics, 37, 273-80, 1996) as evidence that because murine SDF-5 mRNA is present in brain, heart, kidney, lung, and thymus, it cannot be ascertained to have contributed to cartilage formation. Applicants respectfully traverse. The presence of murine SDF-5 mRNA in a variety of tissues does not detract from the utility of SDF-5 in increasing cartilage formation when it is combined with BMP2 as demonstrated in Example 7 of the application.

One utility of the invention is in SDF-5's ability to work additively with BMP-2 to increase cartilage formation. This is described in Example 7 at page 53, lines 10-26 of the application. This is a specific, substantial, and credible utility. Applicants are not required to show more than this.

To demonstrate utility of an invention, it is not necessary to describe the mechanism of cartilage formation, be it through blocking Wnt activity and/or blocking the transition of differentiating chondrocytes into osteoblasts. As stated in the MPEP at 2107 "[i]f the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a 'specific and substantial utility') and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." The real world use of the invention is in the treatment of cartilage disorders as described at page 1, lines 10-14 of the application.

At 2107.01 the MPEP further states "[c]ontrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention." [Emphasis added]. Applicants have identified the biological activity as formation of cartilage and have correlated it to "the treatment of cartilage disorders, such as osteoarthritis, rheumatoid arthritis and articular cartilage defects" (page 1, lines 10-11).

The *in vitro* data disclosed in Example 7 is accepted in the art as being correlated with *in vivo* activity. The model disclosed in Example 7, involving the examination of markers in v-myc oncogene immortalized cell lines from 13-dpc mouse limb (MLB13MYC), is a model accepted by those skilled in the art as being correlated with *in vivo* activity (Rosen et al., J. Bone Miner. Res., 9, 1759-68, 1994 at page 1759). This model has been used for years (see e.g. Gori et al., JBC, 276(49), 46515-22, 2001 and Kearns et al., JBC, 276(45), 42213-8, 2001).

No further experimentation is necessary to show utility. It is well established that *in vivo* activity is not necessary to establish utility. As stated in the MPEP at 2107.01:

> We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility.

Claim Rejections – 35 U.S.C. §112, first paragraph
Claims 18-20, 22, 23, and 29 have been rejected under 35 U.S.C. §112, first paragraph.

The editorial by Dermer (Biotechnology, 12, 320, 1994) cited by the Examiner actually supports the patentability of the instant invention. Dermer states that the use of *in vitro* studies as the foundation for determining whether to proceed with *in vivo* testing is the model generally accepted in the art. According to Dermer (2nd column, first paragraph, pg. 320), "new drugs are selected for human trials because they kill tumor cell lines in the laboratory" thus supporting the fact that *in vitro* testing provides enablement for new drugs. The fact that Dermer does not agree with this method is irrelevant to the patenability of the current invention. Dermer is arguing that the standard methods used in the art and generally accepted accepted by the FDA are unsuitable; such an opinion obviously does not change the patentability of the instant invention. The article is merely an editorial opinion and, further, the subject matter of cancer is not relevant to SDF-5 or any protein related to SDF-5.

The Examiner's citation of a 1983 textbook (Fresney, Culture of Animal Cells: A Manual of Basic Technique, 1st ed., 4, Alan Liss, Inc.), furthermore, does not speak to the understanding of those skilled in the art in 1997. Although Fresney recognizes the differences between *in vitro* and *in vivo* models, he states that "as long as the limits of the model are appreciated, [*in vivo* models] can become a very valuable tool." The Examiner's citation of general editorial references is not enough to overcome the specific evidence presented herein that the experiments disclosed by the Applicants are evidence of *in vivo* activity.

The model disclosed in Example 7 is well known to correlate with *in vivo* activity (Rosen et al., J. Bone Miner. Res., 9, 1759-68, 1994 at page 1759). This model has been used as an acceptable model by those skilled in the art (see e.g. Gori et al., JBC, 276(49), 46515-22, 2001 and Kearns et al., JBC, 276(45), 42213-8, 2001). Rosen states that the specific *in vitro* model used in this application is well correlated to *in vivo* activity and, clearly, this is sufficient to overcome the question of the relevance of the *in vitro* assay used with regard to *in vivo* activity.

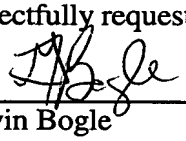
The Examiner's argument that the invention is not enabled based on the inability to show that the sequence binds to the Wnt binding domain is not well taken. The methods used by the Applicants are well known in the art to be a model for the formation of chondrocyte and/or cartilage. Enablement does not require the mechanism by which the frazzled protein causes the formation of chondrocytes and/or cartilage tissue. It is enough that it does cause the formation of chondrocytes and/or cartilage tissue (see page 53 of the application). This point is made clear in *Cross v. Iizuka*, 753 F.2d 1040, 1042 (Fed. Cir. 1985) as "it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."

The MPEP describes the test of enablement as whether undue experimentation is required to make the invention. At 2164.04 of the MPEP, it is stated that a rejection of enablement is based on a specification that "fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." There is no requirement to disclose the underlying mechanism of the invention.

The invention is enabled by virtue of the ability of SDF-5 to induce the formation of chondrocytes and/or cartilage tissue (see, e.g., Example 7, pages 52-53) as proven by models accepted by those skilled in the art. As stated in the MPEP at 2164.01(b), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims, then the enablement requirement of 35 U.S.C. 112 is satisfied."

Based on the foregoing, Applicants request the reconsideration of this application and that it be passed to issue.

Respectfully requested,



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Limited Recognition Under 37 C.F.R. §10.9(b)

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